Journal of Sports Physiology and Athletic Conditioning (J.S.P.A.C) 2025; 5 (15): 1-10

Research Article

The effect of resistance training and testosterone consumption on Caspse3 gene expression in the heart tissue of male Wistar rats

Reihaneh Ghanei[1], Abdolali Banaifar*[2], Ali Garzi[3], Sajad Arshadi[2]

1.PHD student, Department of exercise physiology, South Tehran Branch, Islamic azad university, Tehran, Iran.
2.Associated Professor, Department of exercise physiology, South Tehran Branch, Islamic azad university, Tehran, Iran
3. Associated Professor, Department of Sport Sciences, Faculty of Humanities, University of Zanjan. Zanjan. Iran

Received: 3 February 2025
Revised: 8 March 2025
Accepted: 9 April 2025

Abstract

Background: Studies show that cardiac tissue is one of the tissues that may be damaged as a result of anabolic steroid abuse. The aim of the present study was to study the effect of eight weeks of resistance training and testosterone consumption on the expression of caspase 3 under resistance training in the heart tissue of male Wistar rats.

Materials and Methods: In this study, 21 male Wistar rats (8 weeks old) with a mean weight of 252.20 ± 11.70 g were selected and divided into 3 groups: control, resistance training, and resistance training + testosterone. The resistance training protocol was performed five days a week (four sets of six with a rest of 60 to 90 seconds) in the form of climbing a 1-meter ladder, in which the weights were increased to 60% of the body weight in the first week and 20% of the rats' body weight each week. Testosterone enanthate injection was performed intramuscularly at a dose of 20 mg/kg, 3 days a week. To analyze the research findings, one-way analysis of variance test and Tukey's post hoc test were used to show the difference between groups ($p \geq 0.05$).

Results:
The results showed that the expression of caspase 3 in the exercise + testosterone group increased significantly compared to the control group ($P=0.001$). However, these changes in the exercise group did not show a significant difference compared to the control group ($P \geq 0.05$). Also, no significant change was observed between the two exercise and exercise + testosterone groups ($P \geq 0.05$).

Conclusion: Based on the results of the present study, it can be said that the use of supraphysiological doses of testosterone enanthate along with resistance training can increase apoptotic factors in the heart tissue of rats consuming enanthate and increase the possibility of myocardial damage.

Keywords:
Resistance Training, Caspase 3, Heart tissue, Testosterone Enanthate, Rats

***Corresponding author:** Abdolali Banaeifar
Address: Associated Professor, Department of exercise physiology, STC, Islamic azad university, Tehran, Iran
Email: A.banaeifar@aiu.ir
A B: 0000-0002-4193-7591

Journal of Sports Physiology and Athletic Conditioning

Introduction

Anabolic-androgenic steroids (AAS) are frequently used by athletes as anabolic drugs to enhance sports performance. AAS are compounds derived from testosterone, the primary male hormone, which has long been utilized in medical sciences for treating certain diseases and can be administered in various forms, including oral and injectable (1). The use of AAS to restore or improve impaired physiological functions should be prescribed in precise and controlled doses (2). However, abuse of AAS at high doses far exceeds clinically recommended levels, particularly in non-medical contexts such as body aesthetics and sports performance enhancement, posing a significant challenge (3). Today, nearly all professional and semi-professional athletes use AAS. The global lifetime prevalence of AAS use is estimated at 3.3%, with 6.4% for men and 1.6% for women. However, this varies widely across countries, reaching up to 25% in some cases (4). It has been reported that 87% of performance-enhancing drugs among men and women are testosterone enanthate and testosterone propionate (5).

The adverse effects of AAS abuse are associated with a wide range of side effects on the cardiovascular system, liver, and other tissues (6). The harmful effects of AAS abuse on the heart have increasingly been documented in the literature. Abuse of testosterone leads to serious side effects, including myocardial hypertrophy, myocardial fibrosis, and activation of apoptosis. Apoptosis causes the loss of myocardial cells and ultimately reduces myocardial function (7). Abuse of anabolic-androgenic substances is linked to sudden cardiac death, myocardial infarction, ventricular remodeling, and cardiomyopathy. These events are related to the activation of apoptosis due to AAS abuse. Myocardial death without coronary artery disease or or atherosclerosis has also been attributed to apoptosis induced by AAS (8).

Exposure to supraphysiological doses of steroids can lead to heart weakening and enlargement, causing pathological hypertrophy (9). Damage to heart muscle due to long-term AAS abuse may be irreversible. Irreversible heart failure was reported after six months of treatment in a 31-year-old man who had used AAS for 12 years and growth hormone for one year. The patient had ceased abuse one year before hospital admission. The use of multiple steroid compounds combined with intense exercise appears to exacerbate this condition (10).

A study by Zag and colleagues (2011) showed that 20 hours of exposure to stanozolol induced apoptosis in ventricular myocytes of adult mice under laboratory conditions, accompanied by increased Caspase 3 levels (8). Additionally, a study citing several cases of bodybuilder deaths following myocardial infarction after long-term AAS exposure noted that intense training combined with AAS abuse could lead to apoptotic changes in myocytes and endothelial cells (11). Studies suggest that oxidative stress, apoptosis, and inflammation caused by AAS, regardless of dose or duration of exposure, play a significant role in tissue damage and can be considered an independent risk factor for cardiovascular issues (10).

Apoptosis is a physiological mechanism that eliminates unwanted, damaged, or dangerous cells without harming surrounding tissues and is essential for tissue development and homeostasis (12). Apoptosis occurs through two pathways: the intrinsic pathway, mediated by mitochondria, and the extrinsic pathway, mediated by death receptors on the cell membrane (12). Additionally, AAS can induce apoptosis, leading to the transition from

compensatory cardiac hypertrophy to heart failure. Lopez and colleagues demonstrated that testosterone increases apoptosis in vascular smooth muscle cells through the extrinsic apoptosis pathway via reactive oxygen species (7).

Caspases, as key indicators in apoptosis, play a crucial role in regulating the process. Caspases are classified into initiator caspases (e.g., Caspase 8 and 9), which activate early in the process, and executioner caspases (e.g., Caspase 3 and 6), which are activated later by initiator caspases and trigger the caspase cascade (13). Caspase 3, as the most prominent executioner, performs various functions. Due to its position at the intersection of multiple apoptosis induction pathways, Caspase 3 has gained a special place in apoptosis detection assays. Activation of this important protease by initiator caspases initiates the cell death cascade. For example, this enzyme is responsible for the cleavage and eventual degradation of multiple compounds involved in DNA regulation and repair (12, 13).

On the other hand, epidemiological studies indicate that physical activity reduces the risk of at least 13 different types of cancer and provides evidence of its role in decreasing disease recurrence in various tissues (14). However, intense physical activity has been reported to mediate several factors that may alter apoptosis in different tissues. Currently, evidence exists for exercise-induced apoptosis in lymphocytes and skeletal muscles. For instance, glucocorticoids, removal of growth factors, reactive oxygen species (ROS), increased intracellular calcium levels, and tumor necrosis factor (TNF) are some signals that can induce apoptosis (15).

Numerous studies have explored the impact of physical activity and exercise training on apoptosis. Some researchers have noted that a single session of intense exercise can accelerate apoptosis for up to 48 hours (13). In contrast, moderate and consistent exercise is likely to reduce apoptosis in various tissues (16). While many studies have investigated the effects of exercise and steroids separately, research on the combined effects of training and AAS on apoptosis markers, particularly Caspase 3 in heart tissue, remains limited. Nevertheless, some studies have addressed these issues. For example, Kara and colleagues (2018) demonstrated that stanozolol consumption in Wistar rats caused oxidative stress and stanozolol-induced apoptosis (17). Additionally, a study examining the effects of exercise and anabolic-androgenic steroids on hemodynamic factors, glycogen content, angiogenesis, apoptosis, and heart muscle histology in Wistar rats showed that, compared to the control group, the steroid group exhibited significantly higher blood pressure, heart rate, sympathetic nerve activity, testosterone levels, and cardiac Caspase 3 activity (18).

As mentioned, the use of anabolic compounds, especially among young people and athletes aiming to strengthen muscles and enhance performance, is increasingly prevalent. Testosterone enanthate, due to its long-lasting effect (maintaining elevated plasma testosterone levels for about a week with a single injection), is more commonly used (19). However, studies investigating the effect of testosterone enanthate on Caspase 3, the most critical caspase in the apoptosis process (20), in resistance-trained rats are limited. The present study aims to examine the effects of resistance training and testosterone consumption on the Caspase 3 index in the heart tissue of Wistar rats, potentially providing valuable insights in this area.

2. Materials and Methods

Subjects

This experimental study involved 21 eight-week-old male Wistar rats with an average weight of 220 ± 15 grams, purchased from the Pasteur Institute of Iran and transferred to the laboratory. The animals were housed in washable polycarbonate cages under standard conditions (45-55% humidity, 12:12 light-dark cycle, 23°C temperature) with free access to water and food. Environmental conditions were monitored using ventilation systems, thermometers, and hygrometers to ensure suitability.

Exercise Protocol: One week after acclimatization to the laboratory environment, familiarization training for ladder climbing was conducted for resistance exercise in rodents. The rats were then divided into three groups: control (7 rats), exercise (7 rats), and exercise + testosterone (7 rats). The exercise and exercise + testosterone groups underwent eight weeks of resistance training, five sessions per week (21). This involved four sets of six repetitions with 60-90 seconds of rest, climbing a 1-meter ladder with 26 steps and weights attached to the tails. The weight started at 60% of body weight in the first week, increasing by 20% of body weight weekly. In the fifth week, training intensity was maintained at the fourth week's level to prevent overtraining, and in the final three weeks, it continued at 180% of body weight. The exercise + testosterone group received 20 mg/kg testosterone enanthate (manufactured by Iran Hormone, Iran, serial number 0069) via intramuscular injection three days per week (22). Forty-eight hours after the last training session and testosterone dose, following a 12-hour fast, the rats were anesthetized with a combination of xylazine (3-5 mg/kg) and ketamine (30-50 mg/kg). Their heart tissues were then excised, washed in physiological serum, immediately frozen in liquid nitrogen, and stored at -80°C for variable analysis. Ethical guidelines for working with laboratory animals were followed per the ethics committee's protocol.

Biochemical Analysis of Variables: Caspase 3 gene expression was measured using PCR, with GAPDH as the control gene. The quality and quantity of extracted RNA were assessed using a Nanodrop device. cDNA synthesis was performed using the Takara kit (TAKARA cat NO. 6130) according to the manufacturer's instructions. For RNA extraction, 50 mg of frozen heart tissue was h The average Ct values for replicate samples were calculated, and the comparative Ct method was used to determine relative gene expression levels omogenized, and RNA was extracted using a kit solution per the manufacturer's protocol, purified with DNase I to remove DNA contamination and RNA-degrading enzymes. Two micrograms of mRNA were used to synthesize the first DNA strand. Relative gene expression in the heart was measured using specific primers (Table 1). Primers were designed using Oligo 7 software and blasted on the NCBI website for specificity and accuracy. The 260/280 nm absorbance ratio for extracted samples ranged from 1.8 to 2. RNA quality was verified using 1% agarose gel electrophoresis. Quantitative analysis was conducted using a StepOnePlus real-time PCR system (Applied Biosystems, Foster City, CA, USA). The average Ct values for replicate samples were calculated, and the comparative Ct method was used to determine relative gene expression levels.

3. Results

Statistical analysis

Data normality was assessed using the Shapiro-Wilk test. One-way ANOVA was used to determine significant differences between variables, with Tukey's post-hoc test applied if significant. Statistical analyses were performed at a significance level of $P \geq 0.05$ using SPSS version 26.

The results indicated a significant increase in Caspase 3 expression in the exercise + testosterone group compared to the control group ($P = 0.001$), with exercise + testosterone significantly elevating this index. However, no significant difference was observed in the exercise group compared to the control group, though a non-significant increase was noted. No significant difference was found between the exercise and exercise + testosterone groups ($P = 0.147$) (Figure 1).

Table 1: Primer Sequence Specifications for Each Gene (Caspase 3)

Gene	Forward	Reverse
Caspse3	GGAGTGACTGGAAAGCCGAA	CTTCTGGCAAGCCATCTCCTCA

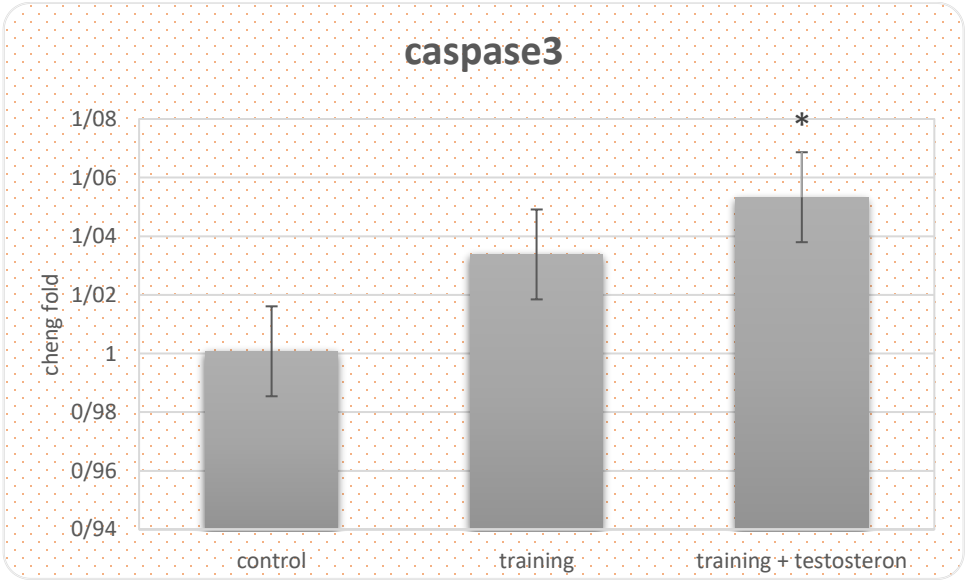

Figure 1: Average Caspase 3 Expression in Study Groups

Discussion

The results of the present study regarding the Caspase 3 index show that resistance training led to a non-significant increase in Caspase 3 expression compared to the control group, while exercise + testosterone resulted in a significant increase. Consistent with this study, Hu and colleagues (2012) demonstrated that 12 weeks of intense aerobic training on a treadmill increased the expression of Caspase 3 and cytochrome C genes related to mitochondrial apoptosis in the cardiac muscle of Wistar rats, potentially exacerbating apoptosis via the intrinsic pathway (23). Similarly, Sharifi and colleagues (2017) found that resistance training at 80% 1RM increased serum P53 and Caspase 3 levels in non-athlete men (24).

One primary hypothesis for apoptosis due to intense exercise is the increased production of ROS from heightened metabolism. Elevated reactive oxygen species can directly cause DNA damage and apoptosis (25). Although ROS indices were not measured in this study, the high intensity of resistance training (up to 180% of body weight) may have increased ROS and Caspase 3 expression in Wistar rats.

The results of Jookar and colleagues (2021) were not aligned with this study, as they found no significant change in Caspase 3 content in diabetic mice after high-intensity interval training compared to the control group. They suggested that training reduced P53 protein content and inhibited Caspase 3 activation, likely deactivating the apoptosis pathway in cardiac cells of type 1 diabetic mice (26). Similarly, Huang and colleagues (2016) showed that 10 weeks of physical training inhibited Fas-dependent and mitochondria-dependent apoptosis pathways in ovariectomized mice, significantly reducing Fas ligand, Caspase 8, and activated Caspase 3 (27). Some studies highlight the protective role of exercise against apoptosis, while others argue that intense exercise may increase apoptotic factors or decrease anti-apoptotic proteins, depending on exercise intensity, duration, type, and the health or fitness status of the subjects (14, 15).

Regarding the effect of exercise + testosterone on Caspase 3, although limited studies exist, some clinical and sports studies align with the present findings, including those by Hasan Asma (2013) and Papamitsou (2011) (18, 28). Hasan Asma and colleagues (2013) showed that exercise and AAS increased cardiac Caspase 3 activity, with histological evidence of pathological cardiomyocyte hypertrophy and mild angiogenesis, suggesting potential cardiac damage from AAS use with exercise (18). Papamitsou (2011) reported that testosterone abuse in Wistar rats caused myocardial hypertrophy, fibrosis, and apoptosis (increased Caspase 3), with nandrolone potentially damaging DNA via ROS. Another experimental study on rabbits treated with 8 mg/kg nandrolone daily for 60 days confirmed increased Caspase 3 activity, supporting the toxic potential of AAS on cardiac tissue (28).

Steroids may also increase pro-fibrotic cytokines like TGF-β in kidney tissue, promoting apoptosis and focal segmental glomerulosclerosis. Environmental and inflammatory stress can cause proteotoxic damage and regulate heat shock proteins. Studies suggest that oxidative stress and free radicals from AAS abuse enhance Caspase 3 activity, potentially altering mitochondrial respiratory chain complexes and monooxygenase systems, leading to an imbalance in free radical production (29-37). AAS exert a pre-apoptotic effect on cardiac myocytes, increasing sarcoplasmic reticulum Ca^{2+} release and mitochondrial permeability,

releasing apoptosis-inducing factors like cytochrome C and Caspases (32, 33).

Various factors, such as TNFα and the renin-angiotensin-aldosterone system (RAAS), activate extrinsic and intrinsic apoptosis pathways, with the angiotensin-converting enzyme 2 (ACE2) playing a key role (34). A study linked ACE2, TNFα, and Caspase 3, showing that testosterone, ACE2, and TNF-α interactions in cultured cardiac myocytes induce apoptosis in a dose-dependent manner .

Conclusion

lthough high-intensity resistance training did not significantly alter Caspase 3 gene expression, a non-significant increase was observed compared to the control group, possibly due to ROS production. However, exercise + testosterone significantly increased Caspase 3 expression, indicating enhanced apoptosis in Wistar rat heart tissue. This suggests that supraphysiological doses of testosterone enanthate with resistance training may increase apoptosis risk, potentially leading to cardiomyopathy and severe cardiac damage. It is recommended to raise awareness among young people, especially athletes, about the risks of combining steroids with resistance training.

Acknowledgements

This article is derived from a doctoral dissertation. The authors express gratitude to all those who contributed to this research.

Funding

This study did not have any funds.

Compliance with ethical standards

Conflict of interest None declared.

Ethical approval the research was conducted with regard to the ethical principles.

Informed consent Informed consent was obtained from all participants.

Author contributions

Conceptualization: A.B., A.G.; Methodology: R.G., S.A.; Software: A.B., R.G., A.G.; Validation: S.A., A.B.; Formal analysis: A.B., A.G; Investigation S.A., A.B., Resources: R.G.; Data curation: A.B., A.G; Writing - original draft: H.S., S.R.; Writing - review & editing: A.B., R.G., A.G.; Visualization: A.B.; Supervision: A.B.; Project administration: A.G.; Funding acquisition: A.B., R.G.

References

1. Abdi Hamzekolai H, Gaeini AA, Kordi MR, Dabidi Roshan V. The monitoring of prolonged effects of anabolic-androgenic steroid on cardiovascular indices in former bodybuilders. Journal of Practical Studies of Biosciences in Sport. 2016 Aug 22;4(7):55-66. https://doi.org/10.22077/jpsbs.2016.383

2. Baytugan NZ, Kandemir HÇ. The effect of anabolic androgenic steroids on heart rate recovery index and electrocardiographic parameters in male bodybuilders. Journal of Electrocardiology. 2024 May 1;84:95-9. DOI: 10.1016/j.jelectrocard.2024.03.015
PMID: 38579637.

3.Bond, P., Smit, D.L. and de Ronde, W., 2022. Anabolic–androgenic steroids: How do they work and what are the risks?. *Frontiers in Endocrinology*, *13*, p.1059473. PMCID: PMC9837614
DOI: 10.3389/fendo.2022.1059473

4. Hammoud S, van den Bemt BJ, Jaber A, Kurdi M. Chronic anabolic androgenic steroid administration reduces global longitudinal strain among off-cycle bodybuilders. International Journal of Cardiology. 2023 Jun 15;381:153-60. DOI: 10.1016/j.ijcard.2023.03.057 PMID: 37003371

5. Sagoe D, Andreassen CS, Pallesen S. The aetiology and trajectory of anabolic-androgenic steroid use initiation: a systematic review and synthesis of qualitative research. Substance abuse treatment, prevention, and policy. 2014 Dec;9:1-4.DOI: 10.1186/1747-597X-9-27
PMCID: PMC4091955.

6. Goldman A, Basaria S. Adverse health effects of androgen use. Molecular and cellular endocrinology. 2018 Mar 15;464:46-55 DOI: 10.1016/j.mce.2017.06.009. PMID: 28606866

7. Lopez P, Radaelli R, Taaffe DR, Newton RU, Galvão DA, Trajano GS, Teodoro JL, Kraemer WJ, Häkkinen K, Pinto RS. Resistance training load effects on muscle hypertrophy and strength gain: systematic review and network meta-analysis. Medicine and science in sports and exercise. 2020 Dec 26;53(6):1206. DOI: 10.1249/MSS.0000000000002585 PMCID: PMC8126497

8. Zaugg M, Jamali NZ, Lucchinetti E, Xu W, Alam M, Shafiq SA, Siddiqui MA. Anabolic-androgenic steroids induce apoptotic cell death in adult rat ventricular myocytes. Journal of cellular physiology. 2001 Apr;187(1):90-5. DOI: 10.1002/1097-4652(2001)9999:9999<00::AID-JCP1057>3.0.CO;2-Y PMID: 11241353

9. Momoh R. Anabolic-androgenic steroid abuse causes cardiac dysfunction. American Journal of Men's Health. 2024 Apr;18(2):15579883241249647. DOI: 10.1177/15579883241249647
PMCID: PMC11062222

10. Angelini G, Pollice P, Lepera ME, Favale S, Caiati C. Irreversible dilated cardiomyopathy after abuse of anabolic androgenic steroids: A case report and literature review. Biomedical Journal of Scientific & Technical Research. 2019;21:16106-11. DOI: *10.26717/BJSTR.2019.21.003648*

11. Cecchi R, Muciaccia B, Ciallella C, Di Luca NM, Kimura A, Sestili C, Nosaka M, Kondo T. Ventricular androgenic-anabolic steroid-related remodeling: an immunohistochemical study. International journal of legal medicine. 2017 Nov;131:1589-95. DOI: 10.1007/s00414-017-1589-3 PMID: 28432434

12. Santagostino SF, Assenmacher CA, Tarrant JC, Adedeji AO, Radaelli E. Mechanisms of regulated cell death: current perspectives. Veterinary Pathology. 2021 Jul;58(4):596-623. DOI: 10.1177/03009858211005537 PMID: 34039100

13. Würstle ML, Laussmann MA, Rehm M. The central role of initiator caspase-9 in apoptosis signal transduction and the regulation of its activation and activity on the apoptosome. Experimental cell research. 2012 Jul 1;318(11):1213-20. DOI: 10.1016/j.yexcr.2012.02.013 PMID: 22406265

14. Moore SC, Lee IM, Weiderpass E, Campbell PT, Sampson JN, Kitahara CM, Keadle SK, Arem H, De Gonzalez AB, Hartge P, Adami HO. Association of leisure-time physical activity with risk of 26 types of cancer in 1.44 million adults. JAMA internal medicine. 2016 Jun 1;176(6):816-25.
DOI: 10.1001/jamainternmed.2016.1548
PMCID: PMC5812009

15. Liu WY, He W, Li H. Exhaustive Training Increases Uncoupling Protein 2 Expression and Decreases Bcl-2/Bax Ratio in Rat Skeletal Muscle. Oxidative medicine and cellular longevity. 2013;2013(1):780719. DOI: 10.1155/2013/780719 PMCID: PMC3556863

16. Vainshtein A, Kazak L, Hood DA. Effects of endurance training on apoptotic susceptibility in striated muscle. Journal of applied physiology. 2011 Jun;110(6):1638-45. DOI: 10.1152/japplphysiol.00020.2011 PMID: 21474699

17. Kara M, Ozcagli E, Kotil T, Alpertunga B. Effects of stanozolol on apoptosis mechanisms and oxidative stress in rat cardiac tissue. Steroids. 2018 Jun 1;134:96-100. DOI: 10.1016/j.steroids.2018.02.004 PMID: 29477345

18. Hassan AF, Kamal MM. Effect of exercise training and anabolic androgenic steroids on hemodynamics, glycogen content, angiogenesis and apoptosis of cardiac muscle in adult male rats. International journal of health sciences. 2013 Jan;7(1):47. DOI: 10.12816/0006020 PMCID: PMC3612416

19. El-hanbuli HM, Abo-sief AF, Mostafa T. Protective effect of silymarin on the testes of rats treated with anabolic androgenic steroid: A biochemical, histological, histochemical and immunohistochemical study. Histol Histopathol. 2017;4(10).

20. Man SM, Kanneganti TD. Converging roles of caspases in inflammasome activation, cell death and innate immunity. Nature Reviews Immunology. 2016 Jan;16(1):7-21. DOI: 10.1038/nri.2015.7 PMCID: PMC4915362

21. Banaeifar A, Gorzi A, Hedayati M, Nabiollahi Z, Rahmani-Moghaddam N, Khantan M. Effect of an 8-week resistance training program on acetylcholinesterase activity in rat muscle. Feyz Journal of Kashan University of Medical Sciences. 2012 Jan 1;16(1).

22. Joksimović J, Selaković D, Jakovljević V, Mihailović V, Katanić J, Boroja T, Rosić G. Alterations of the oxidative status in rat hippocampus and prodepressant effect of chronic testosterone enanthate administration. Molecular and cellular biochemistry. 2017 Sep;433:41-50. DOI: 10.1007/s11010-017-3014-0 PMID: 28342008

23. Ho TJ, Huang CC, Huang CY, Lin WT. Fasudil, a Rho-kinase inhibitor, protects against excessive endurance exercise training-induced cardiac hypertrophy, apoptosis and fibrosis in rats. European journal of applied physiology. 2012 Aug;112:2943-55. DOI: 10.1007/s00421-011-2270-z PMID: 22160250

24. Sharafi H, Rahimi R. The effect of resistance exercise on p53, caspase-9, and caspase-3 in trained and untrained men. The Journal of Strength & Conditioning Research. 2012 Apr 1;26(4):1142-8. DOI: 10.1519/JSC.0b013e31822e58e5 PMID: 22446679

25. Bouviere J, Fortunato RS, Dupuy C, Werneck-de-Castro JP, Carvalho DP, Louzada RA. Exercise-stimulated ROS sensitive signaling pathways in skeletal muscle. Antioxidants. 2021 Mar 30;10(4):537. DOI: 10.3390/antiox10040537 PMCID: PMC8066165

26. Jokar M, Moghadam MS. Effect of 4 weeks of high-intensity interval training on P53 and caspase-3 proteins content in the heart muscle tissue of rats with type 1 diabetes. Journal of Shahid Sadoughi University of Medical Sciences. 2021.

27. Huang CY, Lin YY, Hsu CC, Cheng SM, Shyu WC, Ting H, Yang AL, Ho TJ, Lee SD. Antiapoptotic effect of exercise training on ovariectomized rat hearts. Journal of applied physiology. 2016 Aug 1;121(2):457-65. DOI: 10.1152/japplphysiol.01042.2015 PMID: 27339185

28. Papamitsou T, Barlagiannis D, Papaliagkas V, Kotanidou E, Dermentzopoulou-Theodoridou M. Testosterone-induced hypertrophy, fibrosis and apoptosis of cardiac cells–an ultrastructural and immunohistochemical study. Medical science monitor: international medical journal of experimental and clinical research. 2011 Sep 1;17(9):BR266. DOI: 10.12659/msm.881930 PMCID: PMC3560513

29. Fanton L, Belhani D, Vaillant F, Tabib A, Gomez L, Descotes J, Dehina L, Bui-Xuan B, Malicier D, Timour Q. Heart lesions associated with anabolic steroid abuse: comparison of post-mortem findings in athletes and norethandrolone-induced lesions in rabbits. Experimental and toxicologic Pathology. 2009 Jul 1;61(4):317-23. DOI: 10.1016/j.etp.2008.09.007 PMID: 19027274

30. D'Errico S, Di Battista B, Di Paolo M, Fiore C, Pomara C. Renal heat shock proteins over-expression due to anabolic androgenic steroids abuse. Mini Reviews in Medicinal Chemistry. 2011 May 1;11(5):446-50. DOI: 10.2174/138955711795445934 PMID: 21443506

31. do Nascimento AM, de Lima EM, Boëchat GA, Meyrelles SD, Bissoli NS, Lenz D, Endringer DC, de Andrade TU. Testosterone induces apoptosis in cardiomyocytes by increasing proapoptotic signaling involving tumor necrosis factor-α and renin angiotensin system. Human & Experimental Toxicology. 2015 Nov;34(11):1139-47. DOI: 10.1177/0960327115571766 PMID: 25673179.

32. M Vicencio J, Estrada M, Galvis D, Bravo R, E Contreras A, Rotter D, Szabadkai G, A Hill J, A Rothermel B, Jaimovich E, Lavandero S. Anabolic androgenic steroids and intracellular calcium signaling: a mini review on mechanisms and physiological implications. Mini reviews in medicinal chemistry. 2011 May 1;11(5):390-8. DOI: 10.2174/138955711795445880 PMCID: PMC4416211

33. Liu JD, Wu YQ. Anabolic-androgenic steroids and cardiovascular risk. Chinese medical journal. 2019 Sep 20;132(18):2229-36.
DOI: 10.1097/CM9.0000000000000407
PMCID: PMC6797160

34. Suvakov S, Bonner E, Nikolic V, Jerotic D, Simic TP, Garovic VD, Lopez-Campos G, McClements L. Overlapping pathogenic signalling pathways and biomarkers in preeclampsia and cardiovascular disease. Pregnancy Hypertension. 2020 Apr 1;20:131-6. DOI: 10.1016/j.preghy.2020.03.011 PMID: 32299060

35. Vasilaki F, Tsitsimpikou C, Tsarouhas K, Germanakis I, Tzardi M, Kavvalakis M, Ozcagli E, Kouretas D, Tsatsakis AM. Cardiotoxicity in rabbits after long-term nandrolone decanoate administration. Toxicol Lett. 2016 Jan 22;241:143-51. doi: 10.1016/j.toxlet.2015.10.026. Epub 2015 Nov 2. PMID: 26541207.

36. Ashtary-Larky D, Kashkooli S, Bagheri R, Lamuchi-Deli N, Alipour M, Mombaini D, Baker JS, Ramezani Ahmadi A, Wong A. The effect of exercise training on serum concentrations of chemerin in patients with metabolic diseases: a systematic review and meta-analysis. Arch Physiol Biochem. 2023 Oct;129(5):1028-1037. doi: 10.1080/13813455.2021.1892149. Epub 2021 Mar 2. PMID: 33651961.

37. Takhti M, Riyahi Malayeri S, Behdari R. Comparison of two methods of concurrent training and ginger intake on visfatin and metabolic syndrome in overweight women. Razi Journal of Medical Sciences. 2020;27(9):98-111.